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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,965	02/26/2007	**Jean Gariepy**	MMC.P-002	2679

57381 7590 07/24/2009

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EXAMINER	
STEELE, AMBER D	
ART UNIT	**PAPER NUMBER**
1639	
MAIL DATE	**DELIVERY MODE**
07/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,965	GARIEPY ET AL.	
	Examiner	Art Unit	
	AMBER D. STEELE	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *8-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *April 30, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Status of the Claims

1. Claims 1-23 were filed on September 15, 2006.

The preliminary amendment filed on September 15, 2006 amended claims 3, 7, 16-18, and 23.

The amendment to the claims received on April 24, 2009 amended claims 1, 2, 4-6, 8, 9, and 11-18 and added new claims 24-35.

Claims 1-35 are currently pending.

Claims 1-7 are currently under consideration.

Election/Restrictions

2. Applicant's election with traverse of Group I (claims 1-7) in the reply filed on April 24, 2009 is acknowledged. The traversal is on the ground(s) that Wong et al. and Fitzgerald do not teach an insert introduced in a protease sensitive loop of the A chain of a toxic protein. This is not found persuasive because the presently claimed invention does not require the insert to be introduced in a protease sensitive loop of the A chain of a toxic protein. The presently claimed invention (independent claim 1) requires the following structure: (a) an A chain of a toxic protein which comprises a protease-sensitive loop region (i.e. inherent property of at least some A chains of toxic proteins) and (b) a polypeptide insert comprising at least 2 amino acid residues wherein the polypeptide insert is introduced into the A chain of a toxic protein (i.e. including nonprotease-sensitive loop regions). In addition, dependent claim 6 states that the polypeptide insert can be before or after amino acids 1-239 of the Shiga-like toxin A chain (i.e. polypeptide insert can be added at the N- or C-terminus of the toxin A chain; polypeptide insert can be added

in nonprotease-sensitive loop regions; specification pages 6-7 states that the protease-sensitive loop is present at residues 242-261). Therefore, Wong et al. teach compositions comprising a peptide fragment between 2 and 50 amino acid residues in length fused to therapeutic agents including A chain toxin (i.e. A chain toxin with an N- or C-terminus addition) and (please refer to the entire specification particularly paragraphs 8-9, 11-12, 56; claims 7, 11, 13-14).

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 8-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 24, 2009.

4. Upon further consideration, the species election for Group I is withdrawn.

Potential Rejoinder

5. Applicants elected claims directed to the product. If the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all the criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). **Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to a rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Priority

6. The present application claims status as a 371 (National Stage) of PCT/CA04/00443.

Information Disclosure Statement

7. The information disclosure statement (IDS) submitted on April 30, 2007 is being considered by the examiner.

Sequence Compliance

8. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Figures 2A and 2B and the specification at page 4, line 29 and pages 16-17 (Tables 1-2) contain sequences without proper SEQ ID NOs:. The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. See the objections to the Drawings and Specification below.

Drawings

9. The drawings are objected to because Figures 2A and 2B contain sequences withtou proper SEQ ID NOs: (see MPEP § 2420). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet

submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

10. The abstract of the disclosure is objected to because figures or drawings should not be duplicated in the specification (i.e. including the abstract). Figure 1 is duplicated in the abstract. Correction is required. See MPEP § 608.01(b).

11. The disclosure is objected to because of the following informalities: page 4, line 29 and Tables 1-2 (see pages 16-17) contain sequences without proper SEQ ID NOs:.

Appropriate correction is required.

12. Clarification regarding the disclosure of SEQ ID NO: 1 in the paragraph spanning pages 6-7 is requested. The specification states that the A chain is 293 amino acids in length. However, SEQ ID NO: 1 is 299 amino acids in length. Therefore, are the 6 additional amino acids of SEQ ID NO: 1 part of the A chain, an addition at the N-terminus, an addition at the C-terminus, etc.?

Invention as Claimed

13. A combinatorial protein library comprising a plurality of protein species, each protein species comprising an A chain of a toxic protein in which an insert has been introduced, wherein the A chain of the toxic protein comprises a protease-sensitive loop or region, and wherein the

insert is a polypeptide of varying amino acid sequence having a length of at least 2 amino acid residues and variations thereof.

Therefore, the presently claimed invention requires the following structure: (a) an A chain of a toxic protein which comprises a protease-sensitive loop region and (b) a polypeptide insert comprising at least 2 amino acid residues wherein the polypeptide insert is introduced into the A chain of a toxic protein (i.e. including nonprotease-sensitive loop regions). In addition, dependent claim 6 states that the polypeptide insert can be before or after amino acids 1-239 of the Shiga-like toxin A chain (i.e. polypeptide insert can be added at the N- or C-terminus of the toxin A chain; polypeptide insert can be added in nonprotease-sensitive loop regions).

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, independent claim 1 requires "an A chain of a toxic protein in which an insert has been introduced" which implies that the "insert" is **within** the A chain of a toxic protein. However, dependent claim 6 states that the insert is introduced "before or after amino acids 1-239 of the Shiga-like toxin I A chain" (i.e. including N- or C-terminus additions, not insertions within the A chain of a toxic protein). Therefore, the scope of the presently claimed invention is not clear.

16. Claims 4-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, do the claims require the full-length sequence of SEQ ID NO: 1 with an insert at the designated positions or if only a portion of SEQ ID NO: 1 is required by the claims. Therefore, the scope of the presently claimed invention is not clear.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-3 and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams et al. U.S. Patent 6,080,400 issued June 27, 2000.

For present claims 1-3 and 6-7, Williams et al. teach fusion proteins (i.e. library) comprising Shiga-like toxin I A chain fused to a polyhistidine tags, MBP, flag, or other tags wherein the tags are added at the N-terminus of the A chain (i.e. before residue 1 of SEQ ID NO: 1) and SEQ ID NO: 47 (i.e. 95.6% identity with present SEQ ID NO: 1) which comprises an insert between residues 4 and 5 and another insert between residues 6 and 7 (please refer to the entire specification particularly columns 5-6, 11-12, 16, 18-19, 23, 44-45; SEQ ID NO: 47; see SCORE).

Therefore, the teachings of Williams et al. anticipate the presently claimed invention.

19. Claims 1-3 and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Gariepy et al. WO 99/40185 published August 12, 1999 (provided by applicants in the IDS).

For present claims 1-3 and 6-7, Gariepy et al. teach polypeptide libraries comprising Shiga-like toxin A chain (SEQ ID NO: 1) fused to hexahistidine at the N-terminus (i.e. before residue 1; please refer to the entire specification particularly the abstract; pages 2-3, 5-6, 8, 11, 15; Figure 1).

Therefore, the teachings of Williams et al. anticipate the presently claimed invention.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claims 1-7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 129-145 of copending Application No. 12/088,206. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in

U.S. application 12/088,206 are drawn to combinatorial protein libraries comprising an A chain of a toxic proteins and an insert of at least 2 amino acid residues wherein the A chain is from Shiga-like toxin and the insert is between residues 242 and 261 of Shiga-like toxin A chain.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639